

IN THE CLAIMS:

Please rewrite the current versions of claims 39-41, 43, 45-47 and 51 as follows.

Pursuant to 37 C.F.R. § 1.121, the following is a clean version of the rewritten claims. A marked-up version of the rewritten claims is attached on a separate sheet.

See F1 39. (Once Amended) A staphylokinase derivative having essentially the amino acid sequence as depicted in figure 1 (SEQ ID NO: 1) reactivity with a panel of murine monoclonal antibodies specific towards staphylokinase and having in addition either one or both of the following:

(a) at least one amino acid substituted with Cys, wherein the substitution is introduced at a position outside both the binding epitope and activation epitope of the staphylokinase molecule, and wherein the substitution allows the formation of a homodimeric form of staphylokinase through the formation of an intermolecular disulfide bridge; and/or

E18 (b) polyethylene glycol coupling to an amino acid residue, wherein the coupling is introduced at a position outside both the binding epitope and the activation epitope, resulting in a significantly reduced plasma clearance while maintaining specific activity.

40. (Once Amended) Staphylokinase derivatives as claimed in claim 39 having essentially the amino acid sequence as depicted in figure 1 (SEQ ID NO: 1) in which one or more amino acids have been replaced by another amino acid thus reducing the absorption of SakSTAR (a specific wild-type variant of staphylokinase)-specific antibodies from plasma of patients treated with staphylokinase.

E18
41. (Once Amended) Staphylokinase derivatives as claimed in claim 39 having essentially the amino acid sequence as depicted in figure 1 in which one or more amino acids have been replaced by other amino acids, wherein the specific activity of said derivatives is at least 50% that of the corresponding wild-type staphylokinase.

E19
43. (Once Amended) Staphylokinase derivatives as claimed in claim 39 and listed in Tables 1, 3, 4, 5, 6, 7, 8, 13, 19 and 20, having the amino acid sequence as depicted in figure 1 (SEQ ID NO: 1) thus reducing the absorption of SakSTAR-specific antibodies from plasma of patients treated with staphylokinase, without reducing the specific activity.

E20
45. (Once Amended) Staphylokinase derivatives as claimed in claim 39, wherein the Cys is chemically modified with polyethylene glycol wherein the polyethylene glycol can have a molecular weight of up to 20 kDa.

E21
46. (Twice Amended) The staphylokinase derivatives of claim 45, wherein (a) selected amino acids in the NH₂-terminal region of 10 amino acids (SEQ ID NO: 1 positions 1-10), are substituted with Cys, which is chemically modified with polyethylene glycol and (b) said derivatives are characterized by a significantly reduced plasma clearance and maintained thrombolytic potency upon single intravenous bolus administration at a reduced dose.

E22
47. (Once Amended) Staphylokinase derivative as claimed in claim 46, wherein the Ser in position 2 or 3 (SEQ ID NO: 1) is substituted with a Cys and the Cys is chemically modified with polyethylene glycol having a molecular weight of 5, 10 or 20 kDa.